

EXHIBIT A

**MARKED-UP VERSION OF THE SPECIFICATION
U.S. PATENT APPLICATION NO. 09/518,081**

Replacing the paragraph beginning at page 9, line 3, and ending at page 13, line 24:

It is to be understood that the present invention is not limited to the examples described herein, and other serine protease inhibitors known in the art are used within the limitations of the invention. For example, one skilled in the art can easily adopt inhibitors as described in WO 98/24806, which discloses substituted oxadiazole, thiadiazole, and triazole as serine protease inhibitors. U.S. Pat. No. 5,874,585 discloses substituted heterocyclic compounds useful as inhibitors of serine proteases, including: (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide; (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(2-phenylethyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide; (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(2-methoxybenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide; (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(trifluoromethyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide; (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(methyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-[M]methylpropyl]-L-[P]prolinamide; ([B]benzyloxycarbonyl)-L-[V]valyl-N-[1-(3-(5-(difluoromethyl)-1,2,4-oxadiazolyl)[]carbonyl)-2-(S)-[M]methylpropyl]-L-[P]prolinamide; ([B]benzyloxycarbonyl)-L-[V]valyl-N-[1-(3-(5-(benzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-[M]methylpropyl]-L-[P]prolinamide; ([B]benzyloxycarbonyl)-L-[V]valyl-N-[1-(3-(5-(3-methoxybenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-[M]methylpropyl]-L-[P]prolinamide; ([B]benzyloxycarbonyl)-L-[V]valyl-N-[1-(3-(5-(2,6-difluorobenzyl)-1,2,4-

oxadiazolyl)carbonyl)-2-(S)-[M]methylpropyl]-L-[P]prolinamide; ([B]benzyloxycarbonyl)-L-[V]valyl-N-[1-(3-(5-(trans-styryl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-[M]methylpropyl]-L-[P]prolinamide; ([B]benzyloxycarbonyl)-L-[V]valyl-N-[1-(3-(5-(trans-4-[T]trifluoromethylstyryl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-[M]methylpropyl]-L-[P]prolinamide; ([B]benzyloxycarbonyl)-L-[V]valyl-N-[1-(3-(5-(trans-4-[M]methoxystyryl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-[M]methylpropyl]-L-[P]prolinamide; ([B]benzyloxycarbonyl)-L-[V]valyl-N-[1-(3-(5-(3-[T]thienylmethyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-[M]methylpropyl]-L-[P]prolinamide; ([B]benzyloxycarbonyl)-L-[V]valyl-N-[1-(3-(5-([P]phenyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide; and ([B]benzyloxycarbonyl)-L-[V]valyl-N-[1-(3-(5-(3-[P]phenylpropyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-[M]methylpropyl]-L-[P]prolinamide. U.S. Patent No. 5,216,022 teaches other small molecules useful for the practice of this invention, including: [B](benzyloxycarbonyl)-L-valyl-N-[1-(2-[(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)]carbonyl)-2-(S)-methylpropyl]-L-prolinamide (also known as CE-2072), [B](benzyloxycarbonyl)-L-valyl-N-[1-(2-(3-(methylbenzyl)-1,3,4-oxadiazolyl)]carbonyl)-2-(S)-methylpropyl]-L-prolinamide; [B](benzyloxycarbonyl)-L-valyl-N-[1-(2-(5-(methyl)-1,3,4-oxadiazolyl)]carbonyl)-[2-(S)-methylpropyl]-L-prolinamide; [B](benzyloxycarbonyl)-L-valyl-N-[1-(2-(5-(3-trifluoromethylbenzyl)-1,3,4-oxadiazolyl)]carbonyl)-2-(S)-methylpropyl]-L-prolinamide; ([B]benzyloxycarbonyl)-L-valyl-N-[1-(2-(5-(4-[D]dimethylamino[]benzyl)-1,3,4-oxadiazolyl)]carbonyl)-2-(S)-methylpropyl]-L-prolinamide; [B]benzyloxycarbonyl)-L-valyl-N-[1-(2-(5-(1-naphthyl)-1,3,4-oxadiazolyl)]carbonyl)-2-(S)-methylpropyl]-L-prolinamide; ([B]benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3,4-methylenedioxybenzyl)-1,2,4-oxadiazolyl)]carbonyl)-2-(S)-methylpropyl]-L-prolinamide; [B](benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3,5-dimethylbenzyl)-1,2,4-

oxadiazolyl[] carbonyl)-2-(S)-methylpropyl]-L-prolinamide; ([B]benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3,5-dimethoxybenzyl)-1,2,4-oxadiazolyl[] carbonyl)-2-(S)-methylpropyl]-L-prolinamide; ([B]benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3,5-ditrifluoromethylbenzyl)-1,2,4-oxadiazolyl[] carbonyl)-2-(S)-methylpropyl]-L-prolinamide; ([B]benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-methylbenzyl)-1,2,4-oxadiazolyl[] carbonyl)-2-(S)-methylpropyl]-L-prolinamide; ([B]benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(biphenylmethine)-1,2,4-oxadiazolyl[] carbonyl)-2-(S)-methylpropyl]-L-prolinamide; ([B]benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(4-phenylbenzyl)-1,2,4-oxadiazolyl[] carbonyl)-2-(S)-methylpropyl]-L-prolinamide; ([B]benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-phenylbenzyl)-1,2,4-oxadiazolyl[] carbonyl)-2-(S)-methylpropyl]-L-prolinamide; ([B]benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-phenoxybenzyl)-1,2,4-oxadiazolyl[] carbonyl)-2-(S)-methylpropyl]-L-prolinamide; ([B]benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(cyclohexylmethylene)-1,2,4-oxadiazolyl[] carbonyl)-2-(S)-methylpropyl]-L-prolinamide; ([B]benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-trifluoromethyl dimethylmethylene[])-1,2,4-oxadiazolyl[] carbonyl)-2-(S)-methylpropyl]-L-prolinamide; ([B]benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(1-naphthylmethylene)-1,2,4-oxadiazolyl[] carbonyl)-2-(S)-methylpropyl]-L-prolinamide; ([B]benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-pyridylmethyl)-1,2,4-oxadiazolyl[] carbonyl)-2-(S)-methylpropyl]-L-prolinamide; ([B]benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3,5-diphenylbenzyl)-1,2,4-oxadiazolyl[] carbonyl)-2-(S)-methylpropyl]-L-prolinamide; ([B]benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(4-dimethylaminobenzyl)-1,2,4-oxadiazolyl[] carbonyl)-2-(S)-methylpropyl]-L-prolinamide; 2-[(5-[(B]benzyloxycarbonyl)amino]-6-oxo-2-(4-fluorophenyl)-1,6-dihydro-1-pyrimidinyl]-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl[] carbonyl)-2-(S)-methylpropyl]acetamide; 2-

(5-[A]amino-6-oxo-2-(4-fluorophenyl)-1,6-dihydro-1-pyrimidinyl)-N-[1-(3-(5-[](3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl[]))carbonyl)-2-(S)-methylpropyl]acetamide; 2-[(5-[[B]benzyloxycarbonyl)amino]-6-oxo-2-(4-fluorophenyl)-1,6-dihydro-1-pyrimidinyl)-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl[]))carbonyl)-(S)-2-methylpropyl]acetamide; 2-[(5-[A]amino-6-oxo-2-(4-fluorophenyl)-1,6-dihydro-1-pyrimidinyl)-N-[1-(2-(5-[](3-methylbenzyl)-1,3,4-oxadiazolyl[]))carbonyl)-2-methylpropyl]acetamide; ([P]pyrrole-2-carbonyl)-N-(benzyl)glycyl-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl[]))carbonyl)-2-(S)-methylpropyl]amide; ([P]pyrrole-2-carbonyl)-N-(benzyl)glycyl-N-[1-(3-(5-(3-trifluoromethylbenzyl)[])(-1,2,4-oxadiazolyl)-(S)-methylpropyl]amide; (2S,5S)-5-[A]amino-1,2,4,5,6,7-hexahydroazepino-[3,2,1]-indole-4-one-carbonyl[]-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl[]))carbonyl)-(R,S)-2-methylpropyl]amide; BTD-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl[]))carbonyl)-2-(S)-methylpropyl]amide; (R,S)-3-[A]amino-2-oxo-5-phenyl-1,4[,]benzodiazepine-N-[1-(2-(5-(3-methylbenzyl)[])-1,3,4-oxadiazolyl[]))carbonyl)-2-(S)-methylpropyl]acetamide; ([B]benzyloxycarbonyl)-L-valyl-2-L-(2,3-dihydro-1H-indole)-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl[]))carbonyl)-2-(S)-methylpropyl]amide; ([B]benzyloxycarbonyl)-L-valyl-2-L-(2,3-dihydro-1H-indole)-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl[]))carbonyl)-2-(S)-methylpropyl]amide; [A]acetyl-2-L-(2,3-dihydro-1H-indole)-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl[]))carbonyl)-2-(S)-methylpropyl]amide; 3-(S)-([B]benzyloxycarbonyl)amino)-ε-lactam-N-[1-(2-(5-(3-methylbenzyl)[])-1,3,4-oxadiazolyl[]))carbonyl)-2-(S)-methylpropyl]acetamide; 3-(S)-([A]amino)-ε-[]lactam-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl[]))carbonyl)-2-(S)-methylpropyl]acetamide trifluoroacetic acid salt; 3-(S)-[(4-morpholino[]carbonyl-butanoyl)amino]-ε-[]lactam-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl[]))carbonyl)-2-(R,S)-methylpropyl]acetamide; 6-[4-

[F]fluorophenyl]-ε-lactam-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl[]))carbonyl)-2-(S)-methylpropyl]acetamide; 2-(2-(R,S)-[P]phenyl-4-oxothiazolidin-3-yl)-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl[]))carbonyl)-2-(S)-methylpropyl]acetamide; 2-(2-(R,S)-phenyl-4-oxothiazolidin-3-yl)-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl[]))hydroxymethyl)-2-(S)-methylpropyl]acetamide; 2-(2-(R,S)-[B]benzyl-4-oxothiazolidin-3-yl)-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl[]))carbonyl)-2-(S)-methylpropyl]-acetamide; 2-(2-(R,S)-[B]benzyl-4-oxothiazolidin-3-yl oxide)-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl[]))carbonyl)-2-(R,S)-methylpropyl]acetamide; (1-[B]benzoyl-3,8-quinazolinedione)-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl[]))carbonyl)-2-(S)-methylpropyl]acetamide; (1-[B]benzoyl-3,6-piperazinedione)-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl[]))carbonyl)-2-(S)-methylpropyl]acetamide; (1-[P]phenyl-3,6-piperazinedione)-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl[]))carbonyl)-2-(S)-methylpropyl]acetamide; ([1-(P]phenyl-3,6-piperazinedione)-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl[]))carbonyl)]-2-(S)-methylpropyl]acetamide; 3-([(B]benzyloxycarbonyl)amino]-quinolin-2-one-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl[]))carbonyl)-2-(S)-methylpropyl]acetamide; 3-([(B]benzyloxycarbonyl)amino]-7-piperidinyl-quinolin-2-one-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl[]))carbonyl)-2-(S)-methylpropyl]acetamide; 3-([C]carbomethoxy-quinolin-2-one-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl[]))carbonyl)-2-(S)-methylpropyl]acetamide; 3-([A]amino-quinolin-2-one)-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl[]))carbonyl)-2-(S)-methylpropyl]acetamide; 3-((4-[M]morpholino)aceto)amino-quinolin-2-one-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl[]))carbonyl)-2-(S)-methylpropyl]acetamide; 3,4-[D]dihydro-quinolin-2-one-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl[]))carbonyl)-2-(S)-methylpropyl]acetamide; 1-[A]acetyl-

3-(4-fluorobenzylidene)[]piperazine-2,5-dione-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl[])]carbonyl)-2-(S)-methylpropyl]acetamide; 1-[A]acetyl-3-(4-dimethylamino[]benzylidene)piperazine-2,5-dione-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl[])]carbonyl)-2-(S)-methylpropyl]acetamide; 1-[A]acetyl-3-(4-carbomethoxy[]benzylidene)piperazine-2,5-dione-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl[])]carbonyl)-2-(S)-methylpropyl]acetamide; 1-[A]acetyl-3-[(4-pyridyl)methylene]piperazine-2,5-dione-N-[1-(2-(5-(3-methyl[]benzyl)-1,3,4-oxadiazolyl[])]carbonyl)-2-(S)-methylpropyl]acetamide; 4-[1-[B]benzyl-3-(R)-benzyl-piperazine-2,5[,]dione]-N-[1-(2-[5-(3-methylbenzyl)-1,3,4-oxadiazolyl[])]carbonyl)-2-(S)-methylpropyl]acetamide; 4-[1-[B]benzyl-3-(S)-benzyl[]piperazine-2,5[,]dione]-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl[])]carbonyl)-2-(S)-methylpropyl]acetamide; 4-[1-[B]benzyl-3(R)-benzylpiperazine-2,5[,]dione]-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl[])]carbonyl)-2-(S)-methylpropyl]acetamide; 4-[1-[B]benzyl-3-(S)-benzylpiperazine-2,5[,]dione]-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl[])]carbonyl)-2-(S)-methylpropyl]acetamide; 4-[1-[B]benzyl-3-(S)-benzyl[]piperazine-2,5[,]dione]-N-[1-(3-(5-(2-dimethylaminoethyl)-1,2,4-oxadiazolyl[])]carbonyl)-2-(S)-methylpropyl]acetamide; 4-[1-[M]methyl-3-(R,S)-phenylpiperazine-2,5[,]dione]-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl[])]carbonyl)-2-(S)-methylpropyl]acetamide; 4-[1-[M]methyl-3-(R,S)-phenyl[]piperazine-2,5[,]dione]-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl[])]carbonyl)-2-(S)-methylpropyl]acetamide; 4-[1-(4-[M]morpholino[]ethyl)3-(R)-benzyl[]piperazine-2,5[,]dione]-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl[])]carbonyl)-2-(S)-methylpropyl]acetamide; 5-(R,S)-[P]phenyl-2,4-imidazolidinedione-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl[])]carbonyl)-2-(S)-methylpropyl]acetamide; 5-(R)-[B]benzyl-2,4-imidazolidinedione-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl[])]carbonyl)-2-(S)-

methylpropyl]acetamide; 5-(S)-[B]benzyl-2,4-imidazolidinedione-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl[])]carbonyl)-2-(S)-methylpropyl]acetamide; 5-(S)-[B]benzyl-2,4-imidazolidinedione-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1[],2,4-oxadiazolyl[])]carbonyl)-2-(S)-methylpropyl]acetamide; 5-(R)-[B]benzyl-2,4-imidazolidinedione-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1[],2,4-oxadiazolyl[])]carbonyl)-2-(S)-methylpropyl]acetamide; 1-[B]benzyl-4-(R)-benzyl-2,5-imidazolidinedione-N-[1-(2-(5-(3-methylbenzyl)-1[],3,4-oxadiazolyl[])]carbonyl)-2-(S)-methylpropyl]acetamide; and 1-[B]benzyl-4-(R)-benzyl-2,5-imidazolidinedione-N-[1-(3-(5-(3-trifluoromethyl[]benzyl)-1,2,4-oxadiazolyl[])]carbonyl)-2-(S)-methylpropyl]acetamide; among others.